Corrections in FDA Clinical Briefing Materials for July 27 ODAC Meeting

1) Clinical: Section II. B, Page 6, (Efficacy)

Present text:

"Thirty fewer docetaxel treated patients received post-study chemotherapy compared to LY231514 treated patients (randomized and treated population [RT]).

Correction:

"Nineteen fewer docetaxel treated patients received post-study chemotherapy compared to LY231514 treated patients (randomized and treated population [RT]).

Rationale:

Table 9 on Page 31 of the Clinical Section of the FDA Clinical Review lists 126 LY231514 patients receiving post-study chemotherapy and 107 Docetaxel patients receiving post-study chemotherapy, a difference of 19 patients. Based on Table 10, page 32, it is correct to say that thirty more docetaxel treated patients received no post-study chemotherapy.

The same correction is made in the following locations:

Clinical, Section VI, A, Page 18 (Brief Statement of Conclusions)
Clinical, Section VI, D, Page 35 1st paragraph
Clinical, Section X. A, Page 49 (Conclusions), 1st paragraph

2) Clinical: Section VI, C, Page 28, Primary Efficacy Analysis, (Overall Survival), first paragraph

Present text:

"Two statistical tests for the primary endpoint were defined in the protocol amendment: (1) Test for superiority of alimta relative to docetaxel (H_{0l}: HR $\geq$1), and (2) Test for non-inferiority based on a protocol-defined fixed margin (H_{02}: HR $\geq$1.11)."

Correction:

"Two statistical tests for the primary endpoint were defined in the original protocol: (1) Test for superiority of alimta relative to docetaxel (H_{0l}: HR $\geq$1), and (2) Test for non-inferiority based on a protocol-defined fixed margin (H_{02}: HR $\geq$1.l1)."

Rationale:

The two tests (superiority and non-inferiority based on a protocol-defined fixed margin) were specified in the original protocol used for enrolling patients (JMEI amendment (a) submitted to FDA on February 19, 2001).

3) Clinical, Page 30, Table 7 (Exploratory Analyses of Overall Survival)

Present text:

"Estimate of control effect 0.59"

Correction:

"Estimate of control effect 0.555

Rationale:

FDA lists the estimate of control effect for non-inferiority fraction retention that was used by Lilly as 0.59. Lilly actually used 0.555. (The log estimate of the control effect is 0.59).

4) Clinical, Page 11, 2nd paragraph:

Present text:

"Study JMBR , a second-line NSCLC trial.....(unpublished data)"

Clarification:

Study JMBR is published; (Smit EF, Mattson K, von Pawel J, Manegold C, Clarke S, Postmus PE. ALIMTA (Alimta disodium) as second-line treatment of non-sma1l-cell lung cancer: a phase II study. Ann Oncol 14:455-460, 2003).

5) Clinical Section: Table 2 Pg 20 Study investigators.

Present text:

A Canadian investigator, David Stewart, was footnoted indicating that he was disqualified.

Clarification:

The footnote relating to David Stewart was not correct. He was not disqualified. The correct footnote should have stated that "[a] Scott Laurie replaced David Stewart as Primary Investigator during the trial". Footnote "a" was correctly used for a U.S. investigator, Dr. J.A. Ellerton. Lilly chose to not use data from Dr. Ellerton's site because of regulatory violations at his site (Dr. Ellerton was using a sub-investigator who was on the FDA disqualified list).